Systematic Circular Permutation Analysis for Revealing Essential Elements for Protein Folding

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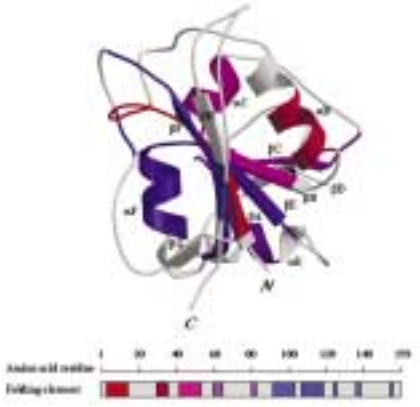
With increasing genomic information by genome projects, it becomes more and more important to reveal the meanings of genomic information in terms of protein structures and functions. However, "protein folding problem", that is, how amino acid sequence determines its tertiary folded structure, has not been solved, and this limits the interpretation of the DNA sequence information. Efforts towards understanding the protein folding problen have mainly focused on native protein. Alternatively, we started to understand the factors that make a sequence foldable or un-foldable. We propose a new concept, "folding elements", which we have investigated by systematic and complete circular permutation analysis. Based on this analysis we conclude that breaking at least one of the folding elements of a native protein abolishes it ability to fold. While a structural approach is important for solving the protein folding problem, it could be misleading since folding elements identified by us do not always correspond to any two- or three dimensional structural elements.



Mapping of the folding elements onto the structure of DHFR. Colored regions represent the folding elements. The location of secondary structure motifs and the N-terminus and C-terminus are also shown.

Reversal of Subjective Temporal Order due to Arm Crossing

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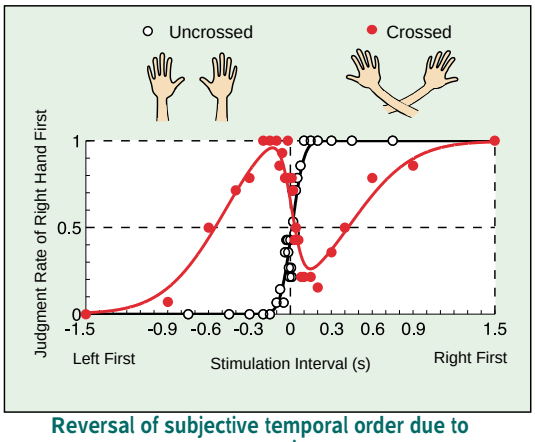
How does the brain order successive events? We have recently shown that crossing the arms caused many subjects to misreport (that is, invert) the temporal order of two stimuli delivered in succession, one to each hand, at moderately short intervals (< 300 ms), though at longer intervals (> 1 s) they generally responded correctly. In contrast, when the arms were uncrossed, the subjects could respond correctly at intervals as short as 70 ms. We conclude that it is not until the spatial locations of the hands are taken into account that the cutaneous signals from the respective hands are ordered in time.



Reversal of subjective temporal order due to arm crossing

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